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A Study of Neuronal Properties, Synaptic Plasticity and Network Interactions
Using a Computer Reconstituted Neuronal Network Derived from Fundamental Biophysical Principles

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Progress Summary

The computer models simulating the biophysical properties of neurons are being implemented on the Macintosh IIci computer. The coding of the neural simulator programs *MacNeur*' and *MacNerveNet* have initiated. The software has gone through the design phase, and is now in the development phase. Based on careful analysis, the design decision was made to implement the neural simulators using object-oriented programming language over the traditional procedural programming la..guage. The choice of Object Pascal language will facilitate future adaptation and modification of the simulators to incorporate newly discovered biophysical properties of neurons in the model without extensively re-writing the programs. Since object-oriented codes are modular in design, the programs can also implement the plastic changes of synaptic substrates in a well-structured organization. The various membrane ionic channels are implemented as "objects" in the same "class", which have similar but unique (biophysical) properties. Thus, a class library can be created to form a collection of different ionic conductance channels, where new (user-specified) channels can be added to the class library. They can then be incorporated into the neural simulators easily using the inheritance-properties of superclass and subclass provided by object-oriented languages.

Modules of the programs are written representing the internal structure of the neural models. These individual modules are currently tested before they are finally integrated into a functioning program. Since the validity of the simulation is crucial, the modules are rigorously tested to ensure a bug-free simulation environment. In summary, the programs have undergone the design phase and are now under the development and validation phase.

Program Development Progress

MacNeuron:

The program *MacNeuron* is the detailed biophysical simulation model of compartmental neurons. The development of the program is divided into three phases to implement the internal representation of the system to be modeled, the control of the simulation, and the external representation of the system to be modeled. The first phase of development is implementing the internal representation of the model since it contains the essence of the neural simulator.

The internal representation of the system has been designed. It contains the essential data structures for representation and algorithms for simulation. The data structures include ionic conductance channels for voltage- and ligand-gated conductances; chemical compartments for species of ions for biochemical reactions, including secondary-messenger systems, to occur; membrane electrical compartments for connecting isopotential regions of membranes for reconstructing the neuron; and linkage structure for connecting neurons together to form a network. The algorithms include the numerical methods for solving the ordinary differential equations representing the electrical compartments and the chemical kinetics reaction equations representing the diffusion of ionic species to-and-from different chemical compartments as well as changes in ionic concentrations due to ionic permeabilities of the conductance channels. The state variables of the equations have been specified and used to represent the internal state of the system. The internal structure of the system is represented by a connected linked-list where unlimited number of compartments can be linked together. Thus the model can be scaled-up to simulate a large-scale system without constraints imposed on by the program. Currently, the size of the model is limited by the available memory of the computer. When Apple Computer Inc. releases the upcoming version 7.0 of the operating system, the program will utilize the virtual memory capability of the computer where it can access up to 4 gigabytes of memory. Currently, the program is still at the development stage of implementing the algorithms for representing the internal structures and numerical integration solutions. Once the system is thoroughly tested, the next phases will be developing the simulation control language and graphical representation of the simulation.

MacNerveNet:

The program *MacNerveNet* is the reduced-system simulation model representing the integrate-and-fire characteristics of neurons for producing spike trains. The program is under development using discrete pulses of spikes representing the spike trains as inputs and outputs of the neurons for processing. Modules of the programs are implemented to represent different synaptic processing functions. The synaptic processing includes Hebbian modification, selective excitation and inhibition for modifiable and non-modifiable synapses. Future anatomical connectivity structures will incorporate statistical receptive field sizes of a specific statistical distribution and statistical connectivity for establishing the synaptic connections. The modules are still under development and being tested,

and when they are thoroughly validated, they will be integrated together to form a single program unit. Once the development of the internal computational codes are completed, the user-interface will be incorporated into the program.

Publications by the Principal Investigator during 1989 and 1990

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Submitted publications

Tam, D. C., Knox, C. K., Friehs, G. M. and Ebner, T. J. Characteristics of visually guided two-dimensional arm movements in the primate with visual feedback alteration. *(submitted to the Journal of Neurophysiology)*

Tam, D. C. Functional significance of bi-threshold firing of neurons. *(submitted to the Society for Neuroscience)*

Tam, D. C. Signal processing by multiplexing and demultiplexing in neurons. *(submitted to Neural Information Processing Systems)*

Publication by Co-Principal Investigator during 1989 and 1990:

Williams, S. and Johnston, D. (1990) Long-term potentiation of hippocampal mossy fiber synapses is blocked by postsynaptic injection of calcium chelators. *Neuron* 3:583-588.

Abstracts

Jaffe, D. B. and Johnston, D. (1989) Voltage-dependence of LTP at the hippocampal mossy fiber synapse. *Society for Neuroscience Abstract* Vol. 15, p. 399.

Williams, S. H. and Johnston, D. (1989) Hippocampal CA3 Mossy fiber LTP is blocked by post-synaptic calcium chelators. *Society for Neuroscience Abstract* Vol. 15, p. 399.